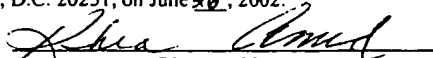


CERTIFICATE OF MAILING BY "FIRST CLASS MAIL"

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to:
Assistant Commissioner for Patents, Washington, D.C. 20231, on June ~~26~~, 2002.


Rhea Amid

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**COPY OF PAPERS
ORIGINALLY FILED**

In the application of:

Nicolaas M.J. VERMEULIN et al.

Serial No.: 09/713,512

Filing Date: November 14, 2000

For: NOVEL POLYAMINE ANALOGUES
AS THERAPEUTIC AND DIAGNOSTIC
AGENTS

Examiner: P. O'Sullivan

Group Art Unit: 1621

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DECLARATION OF REITHA WEEKS UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Reitha Weeks, declare as follows:

1. I have a Ph.D. in Genetics from the University of Washington (1987), completed post doctoral work at Seattle Biomedical Research Institute and Bristol Myers Squibb (Seattle) in the immunology department. I was a senior scientist at Cell Therapeutics, Inc., Seattle, in the molecular biology department before joining Oridigm Corp. (now MediQuest Therapeutics, Inc.) in 1996. I am currently Director of Biological Sciences at MediQuest Therapeutics, Inc., where I coordinate and review scientific projects and manage animal studies.
2. I am familiar with the contents of the above identified U.S. Patent Application 09/713,512 and the Office Action mailed March 26, 2002.

3. I have reviewed the published PCT application by Cherksey et al. (WO 91/00853) and the disclosure concerning lysylspermine, identified as compound "CC" on page 19 therein. The stereochemistry of the lysyl moiety in the lysylspermine compound is not disclosed.
4. I have conducted and/or supervised experiments on tissue concentrations of the L- and D- forms (based upon the stereochemistry of the lysyl moiety) of lysylspermine. Of the two forms, only the D- form is currently within the scope of the pending claims.
5. In those experiments, the L- and D- forms of lysylspermine at a concentration of 0.5 M were delivered via s.c. pump at a rate of 0.5 μ l/hr to nude mice. The daily delivered concentration in the mice was about 150 mg/kg/day and was continued for 13 days, during which time the three mice receiving the L- form of lysylspermine and the four mice receiving the D- form of lysylspermine remained alive. After 13 days, the levels of the L- and D- forms of lysylspermine in liver, kidney, heart and brain tissues were determined in all treated mice.
6. The results, expressed as an average (nmol lysylspermine per gram of tissue) with standard deviation, are shown in the following table.

lysylspermine	liver (nmol/g)	kidney (nmol/g)	heart (nmol/g)	brain (nmol/g)
L- form	17.2 \pm 0.7	180 \pm 17	2.9 \pm 0.8	0.6 \pm 0.4
D- form	187 \pm 28	625 \pm 149	11 \pm 3	1.2 \pm 0.2

7. As shown by the above data, the concentrations of the L- and D-forms of lysylspermine in tissues not protected by the blood-brain barrier are significantly different after 13 days. An increased concentration of the D- form of lysylspermine, in comparison to the L- form, in liver, kidney and heart tissues is an unexpected observation, especially because the compounds only differ in stereochemistry at a single position.
8. The observed higher tissue concentration of the D- form of lysylspermine has significance for the use of the compound in the inhibition of polyamine transport and/or the inhibition of

cell proliferation. Higher tissue concentrations generally permit the use of lower amounts of a compound to achieve the same biological effect in a tissue.

9. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at 2:29 pm on June 24, 2002.

Reitha S. Weeks
Reitha Weeks